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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/532,040	12/30/2005	Brian G. Van Ness	09531-109US1	9035

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EXAMINER	
WEHBE, ANNE MARIE SABRINA	
ART UNIT	PAPER NUMBER
1633	

NOTIFICATION DATE	DELIVERY MODE
05/04/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATDOCTC@fr.com

Office Action Summary	Application No.	Applicant(s)	
	10/532,040	VAN NESS ET AL.	
	Examiner	Art Unit	
	Anne Marie S. Wehbe	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *1/23/09*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29* is/are pending in the application.

4a) Of the above claim(s) *9-29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/23/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment and response received on 1/23/09 has been entered. Claims 1-22 are pending in the instant application. New claims 23-29 have been added. Claims 1-29 are now pending in this application.

Applicant elected without traverse the invention of Group I, and the species Bcl-xl in the responses received on 2/26/08 and 5/28/08. Claims 9-22 were therefore withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Newly submitted claims 23-29 are directed to an invention that is independent or distinct from the invention originally claimed and elected for the following reasons: elected invention I as originally presented was drawn to transgenic rodents, whereas new claims 23-29 are drawn to transgenic rabbits. Rabbits are not rodents. They are part of the order Lagomorpha, not the order Rodentia. Had claims 23-29 been originally presented, they would have restricted from invention I, claims 1-8, as no special technical feature links the inventions and the search and examination of each invention would not be coextensive, see the restriction requirement mailed on 1/8/08 for more details. Since applicant has received an action on the merits for the originally presented and elected invention, claims 23-29 are also withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claims 1-8 are therefore currently under examination. An action on the merits follows. Those sections of Title 35, US code, not included in this action can be found in the previous office action.

Claim Rejections - 35 USC § 112

The rejection of claims 1 and 3-8 under 35 U.S.C. 112, first paragraph, for scope of enablement is maintained in part over claims 1 and 3-8. Applicant's amendment to the claims limiting the transgenic rodent to a transgenic mouse or rat overcomes previously raised issues concerning the lack of enablement for making any and all transgenic rodents. However, applicant's amendments and arguments have not been found persuasive in overcoming the remaining grounds of rejection concerning the lack of enablement for making a transgenic rat whose nucleated cells comprise a transgene comprising an Ig Kappa light chain 3' enhancer operably linked to a nucleic acid encoding Bcl- xl, wherein the transgenic rat exhibits expanded plasma cell and mature B cell populations compared to a wild-type rat.

The previous office action identified the following scope of enablement: a transgenic mouse whose genome comprises a transgene comprising an immunoglobulin kappa 3' enhancer operatively linked to a cDNA encoding Bcl-xL, wherein mature and plasma B cell populations of the transgenic mouse are expanded. Regarding rodents other than a mouse, such as a rat, the previous office explained that the specification does not provide an enabling disclosure for making a transgenic rat with the claimed phenotype of an expanded mature and plasma B cell population. The previous office action stated that the specification provides a working example demonstrating that transgenic mice comprising a Bcl-xl transgene under transcriptional control of the Ig kappa 3' enhancer and kappa promoter exhibit increased numbers of mature B cells and plasma cells. The working examples do not disclose the phenotype of any other transgenic rodent comprising the same or a similar transgene. While the specification, as noted, exemplifies a

transgenic mouse with the claimed phenotype, the state of the art of transgenic at the time of filing was such that the skilled artisan would not have been able to predict whether other species of rodents comprising the same or a similar transgene would have the same phenotype as the disclosed mice. In particular, the previous office action noted that the prior art teaches that the expression of the same gene in different animal species can result in different phenotypes. For example, Mullins teaches that while transgenic rats expressing a Ren-2 gene or HLA B27 exhibit high blood pressure or spontaneous inflammatory disease respectively, the expression of the same genes in mice produced no phenotype (Mullins, page S38). Thus, the skilled artisan would not have been able to predict without undue experimentation whether the expression of Bcl-xL in a rat would be the same as that observed in the disclosed transgenic mice and produce the same phenotype of expanded mature and plasma B cell populations. The applicant has not addressed this issue. As such, the rejection of record as set forth above is maintained.

Claim Rejections - 35 USC § 103

The rejection of claims 1-7 under 35 U.S.C. 103(a) as being unpatentable over Grillot et al. (1996) J. Exp. Med., Vol. 183, 381-391, in view of Adams et al. (1985) Nature, Vol. 318, 533-538, is maintained. Applicant's amendments and arguments have been fully considered but have not been found persuasive in overcoming the rejection for reasons of record as discussed in detail below.

The applicant argues that the rejection is improperly based on conclusory statements without any articulated reasoning or rational underpinning to support the legal conclusion of

obviousness as required by KSR. According to applicants, the conclusion that the Ig heavy chain and the Ig light chain enhancers have similar function is incorrect since in applicant's estimation Adams indicates that the Ig heavy chain enhancer may have greater enhancer activity than the kappa enhancer. In response, it is first noted that the rejection of record is not based on "mere conclusory statements". The motivation to combine the teachings of the Grillot et al. and Adams et al. references was found in the fact that both the Ig heavy chain and Ig kappa chain enhancers had been demonstrated by Adams to be capable of driving B cell specific heterologous transgene expression in transgenic mice such that the substitution of one enhancer with the capacity to drive B cell specific heterologous transgene expression in transgenic mice with another that shares the same property would have yielded the predictable result of transgenic mouse with the claimed features. The rationale to combine the teachings of the references used in the instant rejection is in fact one of the specific rationales set forth in *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385, 1396 (2007). MPEP 2143 sets forth the various rationales identified by KRS. The rationale used in the instant rejection is, " (B) Simple substitution of one known element for another to obtain predictable results". Thus, the rejection of record does not rest on mere conclusory statements.

Second, Grillot et al. only differs from the claimed invention by using an Ig heavy chain enhancer instead of an Ig kappa 3' enhancer. Adams et al. was cited to supplement the teachings of Grillot et al. by teaching that both the Ig heavy chain enhancer and the Ig kappa chain enhancer are effective in driving B cell specific heterologous transgene expression in transgenic mice (Adams et al., pages 533-534 and 537). The rejection of record then stated that since the Ig kappa chain enhancer functions similarly to the Ig heavy chain enhancer in directing B cell

specific expression of heterologous transgenes in transgenic mice, it would have been *prima facie* obvious to the skilled artisan at the time of filing to substitute the Ig kappa enhancer taught by Adams et al. for the Ig heavy chain enhancer in the constructs for making a transgenic mouse according to Grillot et al. with a reasonable expectation of success in using such a construct to produce a transgenic mouse exhibiting a phenotype of expanded mature B cells and plasma cell populations, as such a replacement represents nothing more than simple substitution of one known element for another to obtain predictable results. The functional similarity referred to was the clear demonstration by Adams that both the heavy chain and kappa chain enhancer effectively drive B cell specific heterologous transgene expressing in transgenic mice. The rejection of record did not state or imply that the level of enhancer activity of the heavy chain and kappa enhancer was equivalent or identical, and the rejection of record is not predicated upon equivalent or identical levels of activity. Further, the motivation to combine the teachings of the cited references need not be supported by a finding that the prior art suggested that the combination claimed by the applicant was the preferred, or most desirable combination over the other alternatives. *In re Fulton*, 391 F.3d 1195, 73 USPQ2d 1141 (Fed. Cir. 2004). As such, applicant's arguments are not found persuasive and the rejection of record stands.

The rejection of claim 8 under 35 U.S.C. 103(a) as being unpatentable over Grillot et al. (1996) J. Exp. Med., Vol. 183, 381-391, in view of Adams et al. (1985) Nature, Vol. 318, 533-538, applied to claims 1-7 above, and further in view of Miller et al. (1992) Immunogenetics, Vol. 35, 24-32 is maintained. Applicant's amendments and arguments have been fully

considered but have not been found persuasive in overcoming the rejection for reasons of record as discussed in detail below.

The applicant reiterates their arguments regarding the teachings of Grillot et al. and Adams et al. and further states that Miller et al. does not overcome the deficiencies of Grillot et al. and Adams et al. In response, the arguments regarding the teachings of Grillot et al. and Adams et al. have been discussed in detail above and have not been found persuasive in overcoming the rejection of record. Therefore, the rejection stands.

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (571) 272-0737. If the examiner is not available, the examiner's supervisor, Joseph Woitach, can be reached at (571) 272-0739. For all official communications, the new technology center fax number is (571) 273-8300. Please note that all official communications and responses sent by fax must be directed to the technology center fax number. For informal, non-official communications only, the examiner's direct fax number is (571) 273-0737. For any inquiry of a general nature, please call (571) 272-0547.

The applicant can also consult the USPTO's Patent Application Information Retrieval system (PAIR) on the internet for patent application status and history information, and for electronic images of applications. For questions or problems related to PAIR, please call the USPTO Patent Electronic Business Center (Patent EBC) toll free at 1-866-217-9197. Representatives are available daily from 6am to midnight (EST). When calling please have your application serial number or patent number available. For all other customer support, please call the USPTO call center (UCC) at 1-800-786-9199.

Dr. A.M.S. Wehbé

/Anne Marie S. Wehbé/
Primary Examiner, A.U. 1633